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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,885	03/14/2001	Jennifer L. Hillman	PF-0354-2 DIV	5250

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/26/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/808,885	HILLMAN ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communicati n appears n the cover sh et with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 3-19 are pending.

Claims 4, 7, 9, 18 and 19, drawn to non-elected inventions are withdrawn from examination.

Claims 1 and 2 have been cancelled.

Claims 3, 10 and 13 have been amended.

Claims 3, 5, 6, 8 and 10-17 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

3. Applicants set forth "the refusal to rejoin the process claims with the product claims from which they depend is traversed." Furthermore, Applicants aver "[w]hether the claims of Group II and Group II should be examined together or are properly restricted is a separate issue from whether or not they should ultimately be rejoined."

These remarks are moot until the product claims are allowable. At that time as set forth by *In re Ochiai* and *In re Brouwer* the method claims will be rejoined with the allowable product claims.

Withdrawn Rejections

Claim Rejections - 35 USC § 112

4. The rejection of claim 3 under 35 U.S.C. 112, second paragraph, set forth in Paper number 7 (page 6, paragraph 7a) as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn. Claim 1 has been cancelled.

Claim Rejections - 35 USC § 103

5. The 35 U.S. C. 103(a) rejections of claims 3, 5, 6, 8, 10-14, 16 and 17 under 35 U.S.C. 103(a) as being unpatentable over the secondary references of record in the first action on the merits (Paper number 7) on pages 8-13 are withdrawn in light of the amendment to claim 3.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

6. Claims 3, 5, 6, 8 and 10-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 3 is vague and indefinite in the recitation "biologically-active fragment". It is not clear what activities are bestowed upon these designated fragments described by this term. Accordingly, the metes and bounds of the claim cannot be determined.

Maintained Rejections

Claim Rejections - 35 USC § 112

7. The rejection of claims 3, 5, 6, 8 and 10-17 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention is maintained.

Applicants set forth case law to support their traversal of the instant rejection, as well as cite pages of the specification that allegedly enable the claimed invention. Further arguments include that variants of SEQ ID NO: 1, as well as naturally-occurring amino acids of the said sequence could readily identified without undue experimentation and ultimately the claimed antibodies binding the said sequences could be made. These arguments have been found unpersuasive.

Applicants' disclosure does not provide any guidance as to how to make these sequences with the specific activities activities. Applicants' specification has not evidenced the production of the biologically-active and immunogenic fragments, which would need to be fully characterized before implementing these molecules in therapies and diagnosis of diseases. The specification appears to present an invitation to experiment. Applicants have not identified the 10% of amino acid residues that could be altered, mutagenized or deleted and would continue to yield a sequence retaining

the functional and structural properties of SEQ ID NO: 1 and the antibodies that would bind these variant sequences of SEQ ID NO: 1. The specification discloses only the structural features of SEQ ID NO: 1 (polypeptide) and its corresponding antibodies.

Since the disclosure fails to provide the common attributes or characteristics that identify members of the genus and because the genus is highly variant, the disclosure of the ability to screen is insufficient to describe the genus. One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. Applicants have not provided any guidance as to how to make these divergent sequences, which may possess functions that are not commensurate with the alleged activities of the NABP-1 polypeptides. Applicants' specification has not evidenced the production of antibodies binding such variants, which would need to be fully characterized before implementing these molecules in therapies and diagnosis of diseases. Thus, the specification appears to present an invitation to experiment.

8. The rejection of claims 3, 5, 6, 8 and 10-17 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

Applicants aver that SEQ ID NO: 1 is specifically disclosed in the application and variants of SEQ ID NO: 1 have been described. Applicants set forth that the previous office action misapplied the law, as well as the present claims specifically define the

genus through the recitation of chemical structure, do not define a genus which is "highly variant" and the state of the art at the time of the present invention if further advanced that at the time of previous applications. These arguments have been considered but found unpersuasive.

As noted in the first action on the merits the genus of antibodies binding to naturally –occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO: 1, biologically-active and immunogenic fragments of SEQ ID NO: 1 comprising undefined sequences encompasses a variety of subgenera with widely varying attributes. The specification discloses only the alleged structural features of one species, the polypeptide sequences of SEQ ID NO:1 and its corresponding claimed antibodies. The specification lacks information to lead one of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed.

Claim Rejections - 35 USC § 112/ Claim Rejections - 35 USC § 101

9. The rejection of claims 3, 5, 6, 8 and 10-17 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and a substantial asserted utility or a well established utility is maintained.

Applicants argue that the claimed antibodies are useful as tools for toxicology testing, drug discovery, and the diagnosis of disease and that these uses are "well-established" and have submitted a declaration by L. Michael Furness. It is noted that

toxicology testing and drug discover are not specifically recited in the specification as originally filed.

The similarity of a polypeptide to the corresponding broadly claimed antibodies is not sufficient in demonstrating utility. The substantial likelihood that a protein is functionally related to another polypeptide is not sufficient to base the utility of an unknown protein and give merit to its use toxicology screening. The assertion is made in spite of the lack of disclosure in the instant specification the particulars of toxicology testing with SEQ ID NO:1. Applicants have yet to demonstrate any objective evidence to show NABP-1 causes any disease conditions. One skilled in the art would not only have to see which drugs can change the activity of NABP-1 but they would also have to determine the condition. And clearly undue experimentation would be required to do this.

In order for an antibody to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed antibody and a disease or disorder. The expression of a polypeptide in a tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the cDNA and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed antibodies to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the

polypeptides corresponding to the claimed antibodies are either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed antibodies as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed antibody and the corresponding protein and any disease or disorder and the lack of any correlation between the said polypeptides with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

None of the utilities identified by Applicants, i.e. toxicology testing, drug discovery, disease diagnosis, have been demonstrated to be specific to SEQ ID NO:1. One of ordinary skill in the art must understand how to achieve an immediate and practical benefit from the claimed species based on the knowledge of the class. However, no practical benefit has been shown for the use of SEQ ID NO: 1.

Furthermore, antibodies binding to an isolated polypeptide comprising a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO: 1 is not enabled. Applicants have not provided any guidance as to how to make these divergent sequences, which may possess functions that are not commensurate with the alleged activities of the NABP-1 polypeptides. Applicants' specification has not evidenced the production of such variants, which would need to be

fully characterized before implementing these molecules in therapies and diagnosis of diseases.

As is evidence in the discussions *supra*, each of these factors has been carefully considered in the instant grounds of rejection, and it is maintained that undue experimentation would be required by one of ordinary skill in the art to use the instant invention.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

ALANA HARRIS
PATENT EXAMINER

Alana M. Harris, Ph.D.
March 24, 2003